METHOD AND APPARATUS FOR NONINVASIVELY EVALUATING ENDOTHELIAL FUNCTION

PRIORITY

[0001] This application claims the benefit of U.S. Provisional Patent Application Ser. No. 60/405,352 filed on Aug. 23, 2002, incorporated herein by reference.

FIELD OF INVENTION

[0002] The present invention relates generally to the field of assessing a patient's endothelial function by monitoring changes in hemodynamic parameters responsive to the introduction of a vasodilating stimulant. The monitored hemodynamic parameters may include blood temperature, blood flow, and/or blood oxygen content.

BACKGROUND OF THE INVENTION

[0003] Cardiovascular disease and its sequel account for a significant percentage of the morbidity or mortality in industrialized countries. It is known that cardiovascular disease may be caused and/or enhanced by an impairment of tissue perfusion.

[0004] The endothelium has many important functions in maintaining the patency and integrity of the arterial system. The endothelium can reduce and inactivate toxic superoxides which may be present in diabetics and in smokers. The endothelium is the source of nitric oxide, a local hormone that relaxes the adjacent smooth muscle cells in the media, and is a powerful vasodilator.

[0005] The endothelium regulates vascular homeostasis by elaborating a variety paracrine that act locally in the blood vessel wall and lumen. Under normal conditions, these aspects of the endothelium, hereinafter referred to as "endothelial factors," maintain normal vascular tone, blood fluidity, and limit vascular inflammation and smooth muscle cell proliferation.

[0006] When coronary risk factors are present, the endothelium may adopt a phenotype that facilitates inflammation, thrombosis, vasoconstriction, and atherosclerotic lesion formation. In human patients, the maladaptive endothelial phenotype manifests itself prior to the development of frank atherosclerosis and is associated with traditional risk factors such as

hypercholesterolemia, hypertension, and diabetes mellitus. The maladaptive endothelial phenotype is further identified with emerging risk factors such hyperhomocystinemia, obesity, and systemic inflammation.

[0007] Prior art means for estimating endothelial dysfunction include the use of cold pressor tests by invasive quantitative coronary angiography, measuring the vasodilator response of coronary arteries to acetylcholine, and the injection of radioactive material and subsequent tracking of radiotracers in the blood. These invasive methods are costly, inconvenient, and must be administered by highly trained medical practitioners.

[0008] Noninvasive prior art methods for measuring endothelial dysfunction include, the measurement of the percent change and the diameter of the left main trunk induced by cold pressor test with two dimensional echo cardiography, the Dundee step test, laser doppler perfusion imaging and iontophoresis, high resolution b-mode ultrasound, detection of vascular conditions using an occlusive arm cuff plethysmograph and detection of medical conditions by monitoring the peripheral arterial tone, in conjunction with the creation of hyperemia by the arm cuff.

SUMMARY OF THE INVENTION

[0009] In an embodiment, endothelial function may be assessed by providing a vasodilating stimulant to a patient to stimulate hemodynamic activity in a selected region of the patient's body; monitoring a change in a hemodynamic parameter at the selected region; and assessing the patient's endothelial function based upon said monitoring.

[0010] In a further embodiment, endothelial function may be measured by providing a vasodilating stimulant to a patient to stimulate hemodynamic activity in a selected region of the patient's body; monitoring a change in blood oxygen content at the selected region; and assessing the patient's endothelial function based upon said monitoring.

[0011] In yet a further embodiment, endothelial function may be measured by providing a vasodilating stimulant to a patient to stimulate hemodynamic activity in a selected region of the patient's body; monitoring a change in blood flow rate at the selected region; and assessing the patient's endothelial function based upon said monitoring.

[0012] In one embodiment a self administered endothelial function assessment test is introduced. The test is a non-invasive test for evaluation of endothelial function and can be done without the presence of any medical practitioner. The main endeavor for developing these tests is to enable an ordinary consumer or patient to test their endothelial function and get the information about his endothelial cells, which are responsible for maintaining the patency and integrity of the arterial system. In a self administered fashion this endothelial function assessment kit can be made available in the Check-my heart café, various public places, and also can be made home based.

[0013] This invention helps us in predicting the endothelial dysfunction non-invasively, without the presence of any medical practitioner. Currently available methods require the presence of skilled medical practitioner. These self administered endothelial function assessment tests can be performed at the public places and also at the home. The hospital based tests currently available are costly. The tests mentioned in this invention can be performed in 5-6 minutes. Currently available tests may sometimes require more than 6 minutes for the test.

[0014] .It is emphasized that this summary is not to be interpreted as limiting the scope of these inventions which are limited only by the claims herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] FIG. 1 is a flowchart of a first preferred embodiment of a method of endothelial function assessment;

[0016] FIG. 2 is a flowchart of a second preferred embodiment of a method of endothelial function measurement; and

[0017] FIG. 3 is a flowchart of a second preferred embodiment of a method of endothelial function measurement.

[0018] FIG. 4 is an overall system diagram of the invention, in its preferred embodiment.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS OF THE INVENTION

[0019] As used herein, that which is described as software may be equivalently implemented as hardware.

[0020] Referring now to **FIG. 1**, a preferred method for assessing endothelial function comprises providing a vasodilating stimulant to a patient to stimulate hemodynamic activity in a selected region of the patient's body, illustrated at block **100** in **FIG. 1**; monitoring a change in a hemodynamic parameter at the selected region, illustrated at block **110** in **FIG. 1**; and assessing the patient's endothelial function based upon said monitoring, illustrated at block **120** in **FIG. 1**. In a preferred embodiment, the monitored hemodynamic parameter may be a parameter such as blood temperature, blood oxygen content, blood flow rate, or the like, or a combination thereof.

[0021] Providing a vasodilating stimulant may further comprise compressing the patient's brachial artery for a predetermined period of time and ceasing the compression after that predetermined period of time. Providing a vasodilating stimulant may also comprise occluding blood flow in the patient's arm.

[0022] Additionally, the change in temperature at one of the patient's fingertips may be monitored as may the change in temperature in the patient's arm. Monitoring the change in temperature may be accomplished by placing at least two temperature sensors, for example piezoelectric sensors proximate, e.g. on, the patient's forearm. The temperature sensors may be separated by a known distance.

[0023] Providing a vasodilating stimulant may comprise occluding blood flow in the patient's leg.

[0024] Referring now to **FIG. 2**, in a preferred method for measuring endothelial function comprises providing a vasodilating stimulant to a patient to stimulate hemodynamic activity in a selected region of the patient's body, illustrated at block **200** in **FIG. 2**; monitoring a change in blood oxygen content at the selected region, illustrated at block **210** in **FIG. 2**; and assessing the patient's endothelial function based upon said monitoring, illustrated at block **210** in **FIG. 2**.

[0025] Monitoring may be accomplished by taking measurements with a pulse oximeter. The pulse oximeter may be placed proximate, e.g. on, the tip of one of the patient's fingers.

[0026] Referring now to **FIG. 3**, a second preferred method for measuring endothelial function comprises providing a vasodilating stimulant to a patient to stimulate hemodynamic activity in a selected region of the patient's body, illustrated at block **300** in **FIG. 3**; monitoring a change in

blood flow rate at the selected region, illustrated at block **310** in **FIG. 3**; and assessing the patient's endothelial function based upon said monitoring, illustrated at block **320** in **FIG. 3**.

[0027] Monitoring may be accomplished by taking measurements with a photoplethysmograph placed proximate, e.g. on, one of the patient's fingers. Monitoring may also be accomplished by taking an ultrasound Doppler measurement. Monitoring may occur from a time prior to the beginning of the compression until a time after ceasing, e.g. when blood flow has stabilized.

[0028] Providing a vasodilating stimulant may comprise compressing one of the patient's arteries located in an outer extremity of the patient's body for a predetermined period of time and ceasing the compression after said predetermined period of time. The outer extremity may be a leg, an arm, a wrist, and/or a finger.

[0029] The second preferred method for measuring endothelial function may further comprise plotting measured blood flow as a function of time and/or plotting the change in blood flow as a function of time.

[0030] **FIG. 4** is an overall system diagram of an embodiment of the invention. Hyperemia is simulated by creating an occlusion of the target artery (by inducing cuff pressure on arm, wrist, finger or leg) for some time and then suddenly releasing the occlusion. The changes in the arterial blood flow are monitored before the occlusion and then after the release of occlusion. Different techniques may be used to determine the blood flow through the arteries and may include but are not limited to pulse oximetry, temperature measurements, piezoelectric sensors or auditory sensors. These changes are then used to predict the endothelium dysfunction present if any.

[0031] In one embodiment, a method for self administered endothelial function evaluation is provided comprising: creation of occlusion on the arm, leg, wrist or finger of a person in order to block the arterial blood flow, maintaining of the said occlusion for predetermined time at the predetermined pressure, removing the occlusion after predetermined period, monitoring of the changes in the oxygen content of the blood, temperature of finger tip or the blood flow rate, and prediction of endothelial function (EF) from the analysis of above parameters.

[0032] In one embodiment, monitoring of the changes in the oxygen content of the blood is provided by a pulse oximeter connected to the tip of a finger to continuously monitor the oxygen content of the blood in order to predict endothelial function (EF). In another embodiment, temperature sensors are placed on the tip of the finger, to monitor the blood flow and predict the EF from that. In one embodiment, monitoring is provided by two or more sensors separated by some known distance are placed on the forearm of the person when the occlusion is created in the arm, to determine the blood flow rate. The sensors may be pezio electric sensors, micro phone, pressure etc.

[0033] In one embodiment, monitoring is provided by a photoplethysmograph apparatus placednear the finger to monitor the blood flow. In another embodiment, two or more sensors separated by some distance are placed on the arm or the hand and the impedance between them is continuously monitored. This in tum gives the endothelial function.

[0034] In one embodiment, the blood flow is measured with the help of a Magnetohydrodynamic Acoustic-Resonance Near-Infrared (MAReNIR) technique. In another embodiment, blood flow and the changes in the artery dimensions are monitored by a combined Ultrasound-Doppler technique.

[0035] In one embodiment, hyperemia is simulated by creating an occlusion of the target artery (by inducing cuff pressure by a cuff on arm, wrist, finger or leg) for some time and then suddenly releasing the occlusion. Blood flow is monitored over the course of time right from before the creation of occlusion till the blood flow is normalized after the removal of the occlusion, in order to exactly predict the EF. In one embodiment, blood flow and the change in the blood flow are plotted against the time. These two graphs are further analyzed to give more accurate value of the endothelial function. In one embodiment, a self-administered endothelial function assessment system is provide, which gives a "Risk factor score" to the patient at the end of the test, indicating the amount of risk the user has.

[0036] It will be understood that various changes in the details, materials, and arrangements of the parts which have been described and illustrated above in order to explain the nature of this invention may be made by those skilled in the art without departing from the principle and scope of the invention as recited in the appended claims.

STATEMENT OF INDUSTRIAL USE

[0037] The present invention may be used to assess a patient's endothelial function by monitoring changes in hemodynamic parameters responsive to the introduction of a vasodilating stimulant. The monitored hemodynamic parameters may include blood temperature, blood flow, and/or blood oxygen content.